

## CLAIMS

1. A substantially planar substrate in communication with at least one conducting element, wherein the substantially planar structure comprises at least one nonplanar element for establishing and/or maintaining electrical communication with a cell.  
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2. The substrate of claim 1, wherein the at least one nonplanar element comprises a raised portion having an opening in which a conducting fluid is disposed.
3. The substrate of claim 2, wherein the conducting fluid is in electrical communication with a conducting element.  
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4. The substrate of claim 1, wherein at least a portion of the nonplanar element comprises a conducting surface.
5. The substrate of claim 1, wherein the nonplanar element comprises a nonconducting surface.
6. The substrate of claim 1, wherein least a portion of the substrate comprises a polymer.  
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7. The substrate of claim 6, wherein the polymer comprises an elastomeric polymer.
8. The substrate of claim 1, wherein at least a portion of the nonplanar element comprises a carbon material.  
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9. The substrate of claim 1, wherein the at least one nonplanar element is exposed to fluid flow from a fluid source.
10. The substrate of claim 9, wherein the substrate comprises at least one channel in communication with the fluid source and the fluid source provides fluid to the non-planar element through the at least one channel in the substrate.  
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11. The substrate of claim 2, wherein the substrate is in communication with a pressure source for creating a resistant seal between a surface of the nonplanar element defining the opening and a cell in proximity to the opening.
- 5 12. The substrate of claim 1, wherein the substrate is in communication with a pressure source for creating an electrically resistant seal between a surface of the nonplanar element and a cell in proximity to the surface of the nonplanar element.
13. The substrate of claim 4 or 5, wherein the surface is nonplanar.
- 10 14. The substrate of claim 4 or 5, wherein the surface is protruding or rounded.
15. The substrate of claim 1, wherein the nonplanar element comprises a pipet tip, a capillary, or a micropipet.
- 15 16. The substrate of any of claim 12, wherein the nonplanar element comprises a pipet tip, a capillary, or a micropipet.
17. The substrate of claim 15, wherein the nonplanar element comprises a nonplanar surface for contacting a cell.
18. The substrate of claim 17, wherein the surface is protruding or rounded.
19. The substrate of claim 1, wherein the nonplanar element is removable from the substantially planar substrate.
- 20 20. The substrate of claim 1, wherein the nonplanar element is an integral part of the substantially planar substrate.
21. The substrate of claim 1 or 2, further comprising a voltage source for creating an electrically resistant seal between a surface of the nonplanar element defining the opening and a cell in proximity to the opening.
- 25 22. The substrate of claim 21, wherein the resistance of the seal is at least about 100 Mohm.

23. The substrate of claim 1, wherein the nonplanar element is pyramidal, conical, elliptical, toroidal, or comprises stacked planar elements.
24. The substrate of claim 9, further comprising a cell chamber for receiving fluid from the fluid source and wherein the cell chamber comprises a plurality of the nonplanar elements.
25. The substrate of claim 9, wherein fluid from the fluid source is provided to the cell chamber from one or more channels in the substrate.
26. The substrate of claim 1, wherein at least a portion of a surface of the nonplanar element is hydrophilic.
27. The substrate of claim 10, wherein fluid from the one or more channels creates one or more fluid streams for establishing and/or maintaining an electrically resistant seal between the cell and the opening of the nonplanar element.
28. The substrate of claim 10, further comprising a fluid controlling mechanism to control hydrostatic pressure of at least one channel.
29. The substrate of claim 1, wherein a surface of the nonplanar element is modified by exposure to chemical washing.
30. The substrate of claim 1, wherein a surface of the non-planar element is modified by gas phase chemical deposition.
31. A system comprising a mechanism for providing fluid flow for establishing and maintaining an electrically resistant seal between a cell and a conducting element.
32. The system of claim 31, comprising the conducting element.
33. The system of claim 32, wherein the conducting element is movable relative to the fluid source.
34. The system of claim 32, wherein the conducting element is within the lumen of a housing.

35. The system of claim 32, wherein the housing comprises a micropipet, a pipet tip, a capillary, or a hollow electrode.
36. The system of claim 32, wherein the conducting element comprises a carbon fiber electrode.
- 5 37. The system of claim 34, wherein the lumen comprises a conducting fluid.
38. The system of claim 32, wherein the system further comprises a cell chamber and the conducting element is in electrical communication with the cell chamber.
- 10 39. The system of claim 32, wherein the conducting element is provided in association with a nonplanar element for contacting a cell and wherein the nonplanar element is joined to a substantially planar substrate.
40. The system of claim 39, wherein the nonplanar element is removably joined to the substantially planar substrate.
- 15 41. The system of claim 38, further comprising at least one channel for delivering a cell and/or fluid to the cell chamber.
42. The system of claim 39, further comprising at least one channel for delivering a cell and/or fluid to the nonplanar element.
43. The system of claim 41, further comprising a mechanism for delivering at least one agent to the cell chamber.
- 20 44. The system of claim 42, further comprising a mechanism for delivering at least one agent to the cell chamber.
- 25 45. The system of claim 44, wherein the agent is selected from the group consisting of: protein, DNA, RNA, PNA, a receptor agonist, a receptor antagonist, a neurotransmitter, a neurotransmitter analog, an enzyme inhibitor, an ion channel modulator, a G-protein coupled receptor modulator, a transport inhibitor, a hormone, a peptide, a toxin, an antibody, a pharmaceutical agent, a chemical, a purinergic compound, a cholinergic compound, a serotonergic compound, a dopaminergic

- 5 compound, an anesthetic, a benzodiazepine, a barbiturates, a steroid, an alcohol, a metal cation, a cannabinoid, a cholecystokinin, a cytokine, an excitatory amino acid, a GABAergic agent, a ganglioside, a histaminergic compound, a melatonin, a neuropeptide, a neurotoxin, an endothelins, an NO compound, an opioid, a sigma receptor ligand, a somatostatin, a tachykinin, an angiotensin, a bombesin, a bradykinin, a prostaglandin and combinations thereof.
46. The system of claim 41 or 42, further comprising a mechanism for delivering a cell.
- 10 47. The system of claim 46, wherein the mechanism is selected from the group consisting of: a pressure-varying mechanism, an optical tweezer, a mechanism for electroosmosis, a mechanism for dielectrophoresis, a mechanism for delivering alternating current and a mechanism for delivering a direct current.
- 15 48. The system of claim 32, further comprising a micropositioner for positioning the cell in proximity to the conducting element.
49. The system of claim 38, wherein the system comprises one or more channels for generating at least one fluid stream in the cell chamber.
- 20 50. The system of claim 32, comprising an output channel for delivering fluid to a cell and a drain channel for receiving fluid delivered to the cell, wherein the longitudinal axis of the output channel and the longitudinal axis of the drain channel lie in different planes.
51. The system of claim 50, wherein the different planes are perpendicular to each other.
- 25 52. The system of claim 50, wherein the different planes are parallel to each other.
53. The system of claim 32, comprising an output channel for delivering fluid to a cell and a drain channel for receiving fluid delivered to the cell,

wherein the longitudinal axis of the output channel and the longitudinal axis of the drain channel lie in the same plane.

54. The system of claim 50, wherein fluid delivered from the output channel is received by the drain channel, creating a u-shaped fluid stream.
- 5 55. The system of claim 38 or 39, wherein the system comprises at least one conducting element for establishing electrical communication with a cell.
56. The system of claim 55, wherein the fluid stream generates an electrically resistant seal between a cell-contacting surface in electrical communication with the conducting element and a cell in proximity to the cell-contacting surface.
- 10 57. The system of claim 50, wherein the system further comprises a positioner for positioning a cell in proximity to the fluid stream generated by the output channel and the drain channel.
58. The system of claim 34, wherein the conducting element comprises the cell-contacting surface.
- 15 59. The system of claim 34, wherein the cell-contacting surface is nonplanar surface.
60. The system of claim 50, further comprising a pressure mechanism in communication with the outlet channel and the drain channel for generating a u-shaped fluid stream.
- 20 61. The system of claim 56, wherein the electrical resistance of the seal is at least greater than about 100 Mohm.
62. The system of claim 57, wherein the positioner for positioning the cell comprises a housing defining a lumen and an opening at one end, wherein the portion of the housing defining the opening forms a cell contacting surface and wherein the conducting element is disposed within the lumen of the housing.
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63. The system of claim 32, wherein the system further comprises a detector for recording electrical properties of a cell.
64. The system of claim 32, wherein the system further comprises a mechanism which measures electrical properties.
- 5 65. The system of claim 32, wherein the system further comprises a mechanism for electroporating a cell.
66. The system of claim 32, wherein the system comprises a patch clamp pipette.
- 10 67. The system of claim 32, wherein the conducting element is in electrical communication with a cell chamber.
68. The system of claim 67, wherein the cell chamber comprises at least one nonplanar surface.
69. The system of claim 56, wherein the cell-contacting surface is nonplanar.
70. The system of claim 56, wherein the cell-contacting surface is protruding.
- 15 71. The system of claim 69, wherein the cell-contacting surface is hydrophilic.
72. The system of claim 69, wherein the cell-contacting surface is treated by chemical washing.
- 20 73. The system of claim 72, wherein the cell-contacting surface is treated by gas phase chemical deposition.
74. A method for producing an electrically resistant seal between a cell and a cell-contacting surface comprising exposing the cell to at least one fluid stream.
- 25 75. The method of claim 74, wherein electrical resistance is at least about 100 Mohm.

76. The method of claim 74, further comprising measuring electrical properties of the cell.
77. The method of claim 74, wherein the stream is a u-shaped fluid stream.
- 5 78. The method of claim 74, further comprising measuring the properties before and after exposing the cell to an agent.
- 10 79. The method of claim 78, wherein the agent is selected from the group consisting of: protein, DNA, RNA, PNA, a receptor agonist, a receptor antagonist, a neurotransmitter, a neurotransmitter analog, an enzyme inhibitor, an ion channel modulator, a G-protein coupled receptor modulator, a transport inhibitor, a hormone, a peptide, a toxin, an antibody, a pharmaceutical agent, a chemical, a purinergic compound, a cholinergic compound, a serotonergic compound, a dopaminergic compound, an anesthetic, a benzodiazepine, a barbiturates, a steroid, an alcohol, a metal cation, a cannabinoid, a cholecystokinin, a cytokine, an  
15 excitatory amino acid, a GABAergic agent, a ganglioside, a histaminergic compound, a melatonin, a neuropeptide, a neurotoxin, an endothelins, an NO compound, an opioid, a sigma receptor ligand, a somatostatin, a tachykinin, an angiotensin, a bombesin, a bradykinin, a prostaglandin and combinations thereof.
- 20 80. The method of claim 74, wherein the method further comprises providing a substantially planar substrate in communication with at least one conducting element, wherein the substantially planar structure comprises at least one nonplanar element for establishing electrical communication with a cell and which comprises the cell-contacting surface.
- 25 81. The method of claim 74, wherein the method further comprises applying a voltage pulse at the cell-contacting surface to enhance electrical resistance of the seal.
- 30 82. The method of claim 74, wherein the method further comprises applying pressure at the cell-contacting surface to enhance electrical resistance of the seal.



83. The method of claim 76, wherein the method comprises providing a plurality of fluid streams.
84. The method of claim 83, wherein two or more of the fluid streams contact the cell and one or both streams delivers an agent to the cell.
- 5 85. The method of claim 83, wherein two or more of the fluid streams contact the cell and at least two streams deliver different agents or different concentrations of the same agent.
86. The method of claim 84 or 85, wherein at least one stream delivers a buffer to the cell.

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